

# Prevalence of chronic kidney disease of non-traditional causes in patients on hemodialysis in southwest Guatemala

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### **ABSTRACT**

**Objective.** To document the prevalence of patients on hemodialysis in southwestern Guatemala who have chronic kidney disease (CKD) of non-traditional causes (CKDnt).

**Methods.** This cross-sectional descriptive study interviewed patients on hemodialysis at the Instituto Guatemalteco de Seguridad Social on their health and occupational history. Laboratory serum, urine and vital sign data at the initiation of hemodialysis were obtained from chart reviews. Patients were classified according to whether they had hypertension or obesity or neither. The proportion of patients with and without these traditional CKD risk factors was recorded and the association between demographic and occupational factors and a lack of traditional CKD risk factors analyzed using multivariate logistic regression.

**Results.** Of 242 total patients (including 171 non-diabetics) enrolled in hemodialysis in southwestern Guatemala, 45 (18.6% of total patients and 26.3% of non-diabetics) lacked traditional CKD risk factors. While agricultural work history was common, only travel time greater than 30 minutes and age less than 50 years old were significantly associated with CKD in the absence of traditional risk factors. Individuals without such risk factors lived throughout southwestern Guatemala's five departments.

**Conclusions.** The prevalence of CKDnT appears to be much lower in this sample of patients receiving hemodialysis in Southwestern Guatemala than in hospitalized patients in El Salvador. It has yet to be determined whether the prevalence is higher in the general population and in patients on peritoneal dialysis.

Keywords

Central America; renal insufficiency, chronic; dialysis; Guatemala.

Chronic kidney disease (CKD) of non-traditional causes (CKDnT) has been described in a variety of geographic contexts (1). Two regions where it is

well-documented are the Pacific coast of Central America (hence the term Meso-American Nephropathy, MeN) (1, 2) and the North Central Province of Sri Lanka (1). While little is known about the natural history of this pathology, affected individuals tend to have minimal proteinuria until late in the course of disease (3). Renal biopsies demonstrate tubulointerstitial and glomerular injury patterns (4—6) while serum studies in presumed, early-stage CKDnT show hypokalemia and hyperuricemia (4). The etiology of the epidemic of CKDnT is unknown (1).

In Central America, CKD patients are often young men without traditional risk

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factors (notably, poorly-controlled diabetes, hypertension, and obesity) who live in low-altitude, high-temperature regions and work in labor-intensive jobs (agriculture, and particularly sugar cane harvesting) (7—14). Guatemala's Pacific coast climate and agricultural (i.e. sugar cane), genetic and socio-economic profiles are similar to neighboring El Salvador and Nicaragua (15). In retrospective data describing Guatemalan public health sector patients, dialysis enrollment rates were highest in southwestern Guatemala (16), one of the country's major agricultural regions. Dialysis enrollees were significantly more likely to be male than female in this region (16). Based on the contextual similarities with the broader region and on the high prevalence of young men among those undergoing dialysis treatment, it was reasonable to hypothesize that CKDnT also affected patients in southwestern Guatemala.

Guatemala's largest provider of hemodialysis (HD) is the Instituto Guatemalteco de Seguridad Social (IGSS). IGSS maintains three HD units in southwestern Guatemala (in Escuintla, Retalhuleu, and Mazatenango), and various others that provide dialysis to pafrom the southwest Quetzaltenango and multiple sites in Guatemala City). These patients have progressed to end state renal disease (ESRD), regardless of etiology. This study sought to document the proportion of patients living in southwestern Guatemala and receiving HD through IGSS who had either, both or neither of the traditional CKD risk factors of hypertension and obesity. It focused on the southwest as it is where most CKD patients have been identified in Guatemala and is geographically contiguous to the documented CKDnT epidemic in El Salvador and Nicaragua.

# **MATERIALS AND METHODS**

This cross-sectional descriptive study was designed to determine the prevalence of CKDnT and selected risk factors for MeN in southwestern Guatemala.

# **Study Population**

Patients included in the study were receiving HD for ESRD through IGSS in March 2014, were ≥ 18 years old, and were living in southwestern Guatemala (Retalhuleu, Suchitepéquez, Escuintla,

San Marcos and Santa Rosa departments). Those with a history of diabetes were excluded since it was assumed their ESRD was secondary to diabetic nephropathy (17). IGSS provides both HD and peritoneal dialysis for patients suffering from ESRD but patients enrolled in peritoneal dialysis were excluded due to logistical limitations. No patients receiving dialysis through the public or private healthcare systems were included in this study.

### **Data Collection**

Trained interviewers administered a standardized questionnaire designed by Torres et al. and previously implemented in Nicaragua (7). The questionnaire was reviewed and adapted for use among HD patients and for some Spanish terms that differed in Guatemala. In addition to demographics, it included questions on traditional CKD risk factors and proposed CKDnT risk factors. The latter included use of antibiotics (aminoglycosides, notably gentamicin), pain medicines (nonanti-inflammatory steroidal NSAIDs), previous diagnosis with leptospirosis or use of doxycycline (the treatment of choice for leptospirosis in rural parts of low- and middle-income countries) (18), herbal remedies, employment history (including in the construction and mining industries), pesticide exposure, heat stress, frequent urinary tract infections, and quantity of ongoing urine production. It also included questions about other non-communicable disease (NCD) risk factors, renal disease history, family NCD and renal disease history and socioeconomic status (SES). SES was assessed using a previously validated set of questions developed by the United States Agency for International Development (USAID) (19). Patients were approached during their HD session.

After each patient (or next-of-kin) provided informed consent, he or she was interviewed by one of the authors (TL, EC, EH), all of whom were trained in performing the interviews. The lead author (TL) performed all data entry. Interviews were performed at eight HD units in five cities. Three units were located in southwest Guatemala (Escuintla, Retalhuleu, Mazatenango), one in the northwest (Quetzaltenango), and four in Guatemala City. Interviews were conducted at the northwestern and capital-city units because many newly enrolled

HD patients in southwestern Guatemala face long waiting lists, and are accordingly obliged to travel to these units to receive treatment.

### **Chart Review**

After completing the interviews, IGSS's Electronic Medical Record (EMR) was reviewed to collect data on blood pressure, weight, height, serum laboratory values (diagnostic of and secondary to CKD/ESRD), and urinalysis. The results closest in time to when each individual initiated HD were analyzed (ideally prior to first HD). Glomerular Filtration Rate (eGFR, using the EPI-CKD equation) (20) and body mass index (BMI, kilograms (kg)/height in meters squared (m²)) were calculated for each patient.

### **Case Definition**

Patients were classified as "ever hypertensive" if they met any of the following conditions: 1) previous diagnosis of hypertension (self-report); 2) use of anti-hypertensive medications prior to initiation of HD (self-report); or 3) multiple elevated blood pressure readings prior to receiving HD (chart review). Elevated blood pressure readings after initiation of HD were deemed non-diagnostic due to their association with variables like inter-dialytic weight gain and compliance with dialysis (21). Patients were classified as "ever overweight/obese" if they met any of the following conditions: 1) self-reported previous overweight or obese status; or 2) previously-documented BMI  $> 25 \text{ kg} / \text{m}^2$  (chart review). If a patient had ever been hypertensive or obese, he or she was classified as having traditional CKD risk factors. Those patients with no history of either risk factor were classified as having CKDnT. Additional known risk factors for developing CKD or ESRD could not be accurately screened for at population level in this patient sample and thus were not used for classification.

### **Statistical Analysis**

Mean and standard deviation or median and interquartile range were used to describe continuous variables; frequencies and percentages were used for categorical variables. All reported categorical variables are dichotomous unless otherwise noted.

Binary logistic regression was used to determine odds ratios (OR) for likelihood of having CKDnT. Separate analyses were performed for all patients and for male patients alone (CKDnT has been found to be more common among males) (1). Multiple modeling analyses were performed; the results presented here represent the model judged by the authors to be most accurate. For each variable, an initial univariate analysis was performed using either chi-square or Fisher's exact testing. Variables were selected for inclusion in the final regression models if they were significantly related to presence or absence of traditional CKD risk factors in univariate testing or if strong evidence linked them to CKDnT in other regions of Central America (as defined prior to data collection or analysis). Some variables met both criteria. Logistic regression models intentionally included multiple social factors as CKDnT has been linked to such factors in prior work (3, 22). Models were designed to be as parsimonious as possible to increase precision.

Missing data was less than 3% for each group as 167/171 (97.7%) study patients and 139/142 (97.9%) male patients possessed sufficient data to be included in binary logistic regression models. A two-sided p-value of < 0.05 was considered statistically significant. 95% confidence intervals (CI) are included with all OR.

### **Ethical Considerations**

This study was approved by both the Institutional Review Board of Washington University in St. Louis (#201401116) and the Bioethics Committee of IGSS (no number assigned). All aspects of the study were performed in accordance with the ethical standards of the Helsinki Declaration. All study patients (or nextof-kin) provided written, informed consent to participate in the study. Each patient received a randomly assigned identification number after giving consent. Only this number was included in the final database. The original database linking the patient's name and study number was kept on a passwordprotected computer. Paper questionnaires were kept in a closed cabinet in JB's office.

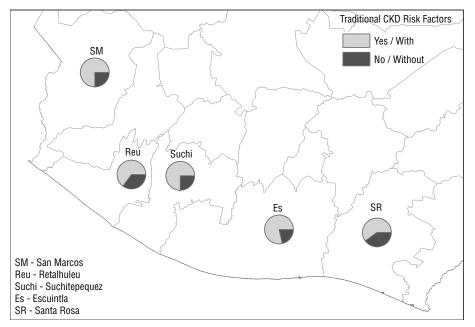
### **RESULTS**

A total of 242 individuals living in southwestern Guatemala received HD at IGSS facilities in March 2014. Of this group, 197 (81.4%) reported that they met the study's inclusion criteria. Of the latter, 195 (99.0%) agreed to be interviewed; both individuals who refused cited a lack of desire to participate. Chart review indicated that only 178 interviewed patients (91.3%) truly met the inclusion criteria; the remaining 17 either received HD

through the private health sector (i.e. they were not IGSS patients despite receiving dialysis at IGSS facilities) or had a previous history of diabetes or both. Additionally, seven patients who met the inclusion criteria had to be excluded as it was not possible to determine whether they had traditional CKD risk factors, leaving a final sample of 171 patients (70.7% of the total). Of these, most (126, 73.6%) had traditional CKD risk factors. The remaining 45 (26.3%) were classified as having CKDnT. Patients with CKDnT were found at all HD units where interviews were performed and lived throughout southwestern Guatemala (Figure 1), with the highest proportions in Retalhuleu and Santa Rosa. The proportion of individuals with traditional CKD risk factors did not vary significantly across surveyed sites, either for all patients (p = 0.38) or for males only (p = 0.69).

Patients with and without traditional CKD risk factors were not significantly different with respect to sociodemographic characteristics (except for years of schooling), past medical history, or other chronic disease risk factors. The percentage of patients with primary school or less was significantly higher among those without traditional CKD risk factors than those with (86.7% versus 66.7%, p = 0.01). Most patients, with or without traditional CKD risk factors, were diagnosed before 50 years of age (median age: 39 years old; interquartile range: 27 to 52 years old). The percentage of patients with a relative that had worked in agriculture was significantly higher among those without traditional CKD risk factors than those with (73.3% versus 52.4%, p = 0.02), while the percentage of patients with a relative diagnosed with hypertension was much lower (17.8% versus 32.0%, p = 0.07) (Table 1). Analyses encompassing only male patients yielded similar results. Although not statistically significant, the proportion of patients under 50 years of age was higher in those without traditional CKD risk factors compared to those with such factors (68.3% versus 52.5%, p = 0.08). Likewise, limited schooling (90.2% versus 70.3%, p = 0.01), travel time greater than 30 minutes to HD (95.0% versus 73.7%, p = 0.004), and family history of agricultural work (75.6% versus 57.4%, p = 0.04) were significantly more common among those without compared to those with traditional CKD risk factors.

FIGURE 1. Prevalence of study participants with and without traditional risk factors for chronic kidney disease (CKD). Guatemala, 2014.



Source: Prepared by the authors from study results.

Most patients traveled more than 30 minutes to receive HD (Table 1, Figure 2). Nearly all (42/44, 95.5%) patients without traditional CKD risk factors had to travel more than 30 minutes compared with 74.2% (92/124) of those with traditional CKD risk factors (p < 0.01).

Proposed CKD risk factors were also assessed. Patients without traditional

risk factors were significantly more likely to have a history of agricultural employment than those with traditional risk factors (77.8% versus 59.5%, p=0.03). Likewise, those without traditional risk factors were more likely to have been working for more than 20 years in agriculture (62.9% versus 38.7%, p=0.02). Similar trends were observed among male patients alone,

TABLE 1. Characteristics of non-diabetic patients from southwestern Guatemala receiving hemodialysis through IGSS and included in the study sample. Guatemala, 2014

	Traditional CKD <sup>a</sup> Risk Factors				
Variable <sup>b</sup>	With (n, %)	Without (n, %)	Р		
Personal characteristics	'				
Sex			0.09		
Men	101 (80.2%)	41 (91.1%)			
Women	25 (19.8%)	4 (8.9%)			
Age (years)	70 (57 10/)	00 (71 10/)	0.10		
< 50 ≥ 50	72 (57.1%) 54 (42.9%)	32 (71.1%) 13 (28.9%)			
Socioeconomic status°	J4 (42.3 /0)	13 (20.970)	0.53		
Socioeconomic Status <sup>-</sup> ≤ 4	25 (20.0%)	11 (24.4%)	0.55		
≥ 5	100 (80.0%)	34 (75.6%)			
Schooling	(**************************************	0 ( ( 0 0 0 7 0 )	0.01		
Primary or less	84 (66.7%)	39 (86.7%)	0.01		
Secondary or more	42 (33.3%)	6 (13.3%)			
Medical / renal history	, ,	,			
Frequent use of NSAIDs <sup>d</sup>			0.47		
≥ 2 times / week	35 (27.8%)	10 (22.2%)	0.17		
< 2 times / week	91 (72.2%)	35 (77.8%)			
Low birth weight			0.81		
Yes	15 (12.2%)	6 (13.6%)			
No	108 (87.8%)	38 (86.4%)			
Ever consumed alcohol			0.67		
Yes	91 (72.2%)	34 (75.6%)			
No	35 (27.8%)	11 (24.4%)			
Ever tried smoking			0.45		
Yes	64 (51.2%)	26 (57.8%)			
No	61 (48.8%)	19 (42.2%)			
Age at diagnosis (years)	( )		0.60		
≤ 50	93 (73.8%)	35 (77.8%)			
> 50	33 (26.2%)	10 (22.2%)	0.04		
Travel time to dialysis (minutes) > 30	92 (74.2%)	40 (OF E0/ )	<0.01		
> 30 ≤ 30	32 (25.8%)	42 (95.5%) 2 (4.5%)			
Family history	02 (20.070)	2 (4.070)			
• •			0.04		
Renal issues Yes	19 (15.1%)	7 (15.6%)	0.94		
No	107 (84.9%)	38 (84.4%)			
Hypertension	107 (01.070)	00 (01.170)	0.07		
Yes	40 (32.0%)	8 (17.8%)	0.07		
No	85 (68.0%)	37 (82.2%)			
Diabetes	,	,	0.41		
Yes	36 (28.6%)	10 (22.2%)	V. 11		
No	90 (71.4%)	35 (77.8%)			
Agriculture			0.02		
Yes	66 (52.4%)	33 (73.3%)			
No	60 (47.6%)	12 (26.7%)			

Source: Prepared by the authors from study results.

where those without traditional risk factors were more likely than those with such factors to have a history of agricultural employment (85.4% versus 69.3%, p = 0.05) and a long duration of agricultural employment (62.9% versus 41.4%, p = 0.04). Fifty-two men (37%) reported having worked in the sugar cane industry, with no significant differences between those with and without traditional risk factors (Table 2). Pesticide use was high among all patients and for men only, but was not significantly associated with a lack of traditional risk factors in either group. For other proposed CKDnT risk factors like NSAID, antibiotic or herbal medicine use, leptospirosis, previous work in the construction or mining industries, frequent urinary tract infections and quantity of ongoing urine production, no significant differences were observed between those without and with traditional CKD risk factors, both for all patients and for men only.

In multivariate, binary logistic regression analyses, only age and travel time to dialysis unit retained significant associations with a lack of traditional CKD risk factors (Table 3). Compared to those 50 years of age or older, younger patients had significantly higher odds of absence of traditional CKD risk factors (OR 2.65, 95% CI 1.14 – 6.13). Those who traveled more than 30 minutes to a dialysis unit also had higher odds of absence of traditional CKD risk factors (5.41, 1.15 - 25.39). Gender, years of schooling, agricultural work, and family history of hypertension or agricultural work were not significantly associated with absence of traditional CKD risk factors. Similar trends were seen among only male patients.

With respect to laboratory-diagnosed abnormalities at HD initiation, only hyperphosphatemia (phosphate > 5.5 mg/dL) was significantly higher among patients with traditional CKD risk factors (52.4%) compared to those without (33%, p = 0.03). When only men were analyzed, the difference in hyperphosphatemia remained but was no longer statistically significant (52.5% versus 36.6%, p = 0.09). Likewise, there were no significant differences in urinary presence of leucocytes (p = 0.29) or proteinuria (p = 0.29) among those with and without traditional risk factors; this was also true in only male patients (p = 0.62and p = 0.14, respectively).

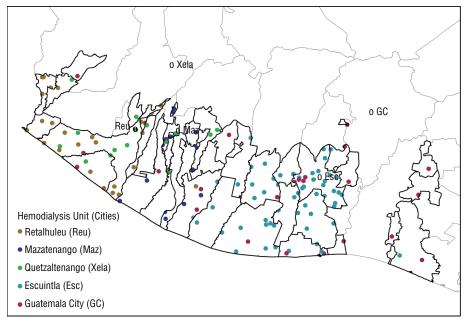
<sup>&</sup>lt;sup>a</sup> CKD: Chronic kidney disease.

<sup>&</sup>lt;sup>b</sup> Total sample size (n) = 171, but samples for individual variables may be smaller due to missing data.

<sup>&</sup>lt;sup>c</sup> Socioeconomic status assessed using USAID questionnaire (19).

d NSAIDs: Non-steroidal anti-inflammatory drugs.

FIGURE 2. Locations of hemodialysis units and patient homes. Guatemala, 2014.



Source: Prepared by the authors from study results.

TABLE 2. Agricultural work history among non-diabetic hemodialysis patients with and without traditional risk factors for chronic kidney disease. Guatemala, 2014

	Traditional CKD <sup>a</sup> Risk Factors							
		All Patients <sup>b</sup>			Men Only <sup>c</sup>			
	With (n, %)	Without (n, %)	р	With (n, %)	Without (n, %)	р		
Agricultural work			0.03			0.05		
Ever	75 (59.5%)	35 (77.8%)		70 (69.3%)	35 (85.4%)			
Never	51 (40.5%)	10 (22.2%)		31 (30.7%)	6 (14.6%)			
Years workedd			0.02			0.04		
> 20	29 (38.7%)	22 (62.9%)		29 (41.4%)	22 (62.9%)			
≤ 20	46 (61.3%)	13 (37.1%)		41 (58.6%)	13 (37.1%)			
Age at start (years)d			0.12			0.11		
≤ 15	52 (69.3%)	19 (54.3%)		49 (70.0%)	19 (54.3%)			
> 15	23 (30.7%)	16 (45.7%)		21 (30.0%)	16 (45.7%)			
Sugar cane			0.33			0.63		
Yes	36 (28.6%)	16 (36.4%)		36 (35.6%)	16 (40.0%)			
No	90 (71.4%)	28 (63.6%)		65 (64.4%)	24 (60.0%)			
Pesticide used			0.37			0.83		
Yes	58 (78.4%)	30 (85.7%)		58 (84.1%)	30 (85.7%)			
No	16 (21.6%)	5 (14.3%)		11 (15.9%)	5 (14.3%)			

Source: Prepared by the authors from study results.

# **DISCUSSION**

This study found that nearly 1 in 5 patients enrolled in HD through IGSS living in southwestern Guatemala lacked traditional CKD risk factors and therefore possibly suffered from

CKDnT. Importantly, some uncommon etiologies of CKD and ESRD are not easily diagnosed in Guatemala at this time; thus, it cannot be categorically asserted that all those without traditional risk factors for CKD have CKDnT, though many likely do. Moreover, in

this sample, patients without traditional CKD risk factors could not be readily distinguished from patients with traditional CKD risk factors on the basis of laboratory abnormalities at HD initiation.

The southwestern cities of Mazatenango (population 100 138), Retalhuleu (population 89 832), and Escuintla (population 158 456), where IGSS maintains HD units, are small compared to Guatemala City (population 993 815) (23). A travel time of greater than 30 minutes is likely the result of a patient traveling from a rural area or of recent initiation on HD, which occasionally requires a lengthy journey to a larger city (Quetzaltenango or Guatemala City) until an HD machine becomes available at a local unit. It is also possible that a combination of both is yielding this longer travel time. The percentage of patients traveling more than 30 minutes to HD was significantly higher among those without traditional CKD risk factors and was a significant predictor of the lack of such factors in multivariate analyses. This is consistent with data from Nicaragua (7-9, 24), El Salvador (11, 12, 25), and Costa Rica (26, 27) describing CKDnT as a disease largely confined to rural

Patients without traditional CKD risk factors were younger compared to those with traditional CKD risk factors. Even though age (less than 50 years old) remained significant in multivariate analyses, it is not possible to assess how much of this difference reflects the epidemiology of hypertension and obesity in Guatemala, where both are more prevalent among the elderly (28). However, CKDnT is a recently-described phenomenon, with the earliest references dating to the early 2000s (14). Whether CKDnT is a new disease, an old disease which is only now coming to the attention of the medical system, or a new and different manifestation of an older disease that now presents clinically in younger patients—perhaps due to new occupational hazards (13), increased temperatures due to global warming (29), or other unidentified risk factor(s)—remains unknown. It is also possible that CKDnT may lead to renal failure and premature death prior to 50 years of age, such that these older individuals would not be represented in this cross-sectional sample. While no regional data is available concerning age

<sup>&</sup>lt;sup>a</sup> CKD: Chronic Kidney Disease.

<sup>&</sup>lt;sup>b</sup> Total sample size (n) = 171, but samples for individual variables may be smaller due to missing data.

<sup>&</sup>lt;sup>c</sup> Total "Men Only" sample size (n) = 142, but samples for individual variables may be smaller due to missing data.

d Sample includes those who reported ever working in agriculture; i.e., for all patients (n) = 110, while for "men only" (n) = 105. Samples for individual variables may be smaller due to missing data.

TABLE 3. Factors associated with a lack of traditional chronic kidney disease risk factors in binary logistic regression among non-diabetic patients receiving hemodialysis through IGSS. Guatemala, 2014

	All Patients <sup>a</sup>			Men Only <sup>b</sup>				
Variable			95 % CI°				95 % CI	
	P	OR <sup>d</sup>	Lower Limit	Upper Limit	P	OR	Lower Limit	Upper Limit
Sex								
Men	0.25	2.18	0.57	8.31	n.a.	n.a.	n.a.	n.a.
Women		Refe						
Age (years)								
< 50	0.02	2.65	1.14	6.13	0.02	2.68	1.15	6.25
≥ 50		Ref				Ref		
Schooling								
Primary or less	0.18	2.16	0.71	6.63	0.12	2.88	0.76	10.84
Secondary or more		Ref				Ref		
Agricultural work								
Ever	0.83	0.85	0.20	3.59	0.98	0.98	0.19	4.93
Never		Ref				Ref		
Family history of hypertension								
Yes	0.22	1.77	0.71	4.42	_ f	_	_	_
No		Ref						
Family History of Agricultural Work								
Yes	0.75	1.28	0.28	5.92	0.99	0.99	0.13	7.61
No		Ref				Ref		
Travel Time to Dialysis								
≤ 30 minutes	0.03	5.41	1.15	25.39	0.05	4.88	1.02	17.19
> 30 minutes		Ref	****			Ref		

Source: Table 3 prepared by the authors from study results.

at death from renal disease, Guatemala is among the Latin American countries with the highest rates of CKD and renal failure mortality in the region (30).

Hypokalemia and hyperuricemia have been described in a limited case series of patients with presumed early-stage CKDnT (4). Among serum or urinary laboratory abnormalities at HD initiation, we found only hyperphosphatemia to be more common in patients with traditional CKD risk factors. While hyperphosphatemia is almost universal in patients with ESRD (31), the significance of this difference in our patient population at HD initiation is unclear. This difference may serve as a surrogate marker of better nutritional status among those with traditional CKD risk factors as protein-rich foods tend to be high in phosphate (32). However, this hypothesis requires further research.

Patients without traditional CKD risk factors (who are possibly affected by CKDnT) were found throughout the hot

and humid southwestern departments of Guatemala. The prevailing economic activity in these departments is agriculture (including sugar cane). This pattern is consistent with the higher rates of dialysis enrollment and the higher proportion of male enrollees documented in patients receiving either HD or peritoneal dialysis through the public health sector in southwestern Guatemala (16). This region is contiguous with the Pacific Coasts of Nicaragua (7-9, 24), El Salvador (11, 12, 25), and Costa Rica (26, 27) where CKDnT has been previously reported.

This study has strengths and limitations. To the best of the authors' knowledge, this is the first study to include blood and urine values from individuals with possible CKDnT at the time of dialysis enrollment, including not just markers of renal function but also values assessing systemic changes secondary to renal disease. The questionnaire used here has been previously implemented in Central America (7, 10), but

only in community-based prevalence surveys, which limits their comparability to the results here, which are only for dialysis patients. A chart review was also used to validate certain key portions of the questionnaire including previous history of hypertension, diabetes or obesity, minimizing individual recall bias. However, the study only included IGSS HD patients, limiting the potential sample. Specifically, a patient must be employed in the Guatemalan formal economy for more than four consecutive months in order to be eligible for healthcare at IGSS; only 33% of Guatemalans are covered (33). Consequently, these results are not generalizable to those in the public or private healthcare systems or those enrolled in peritoneal dialysis through IGSS. The study is also subject to the basic limitations of all cross-sectional studies. As well, some charts lacked information on several variables of interest, making our total sample different for some analyses. Finally, it was not possible to assess how

<sup>&</sup>lt;sup>a</sup> Sample size for "All Patients" analyses (n) = 167 patients for whom all necessary data was available.

<sup>&</sup>lt;sup>b</sup> Sample size for "Men Only" analyses (n) = 139 male patients for whom all necessary data was available.

<sup>&</sup>lt;sup>c</sup> CI: Confidence interval.

d OR: Odds Ratio.

e Ref: Reference variable.

f Insufficient data available to complete this analysis.

differences in age between those with and without traditional CKD risk factors may have affected laboratory values at HD initiation.

### Conclusions

Even though the prevalence of CKD among males in southwestern Guatemala has been previously documented (16), this is the first time the prevalence of CKDnT has been estimated for this region. Despite the much lower prevalence of a lack of traditional risk factors (compared to that in hospitalized CKD patients in El Salvador), one quarter of patients receiving HD are likely to have CKDnT. A long-term cohort study is needed to determine CKDnT incidence,

natural history and risk factors in Guatemala.

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Conflicts of Interest. Dr. Rothstein has worked as a consultant for Gambro Corporation and as a paid speaker for Fresenius Medical Care, Amgen and American Regent. Dr. Joaquin Barnoya receives additional support from an unrestricted grant from the American Cancer Society and the Foundation for Barnes & Jewish Hospital. All other authors report no conflicts of interest.

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### **REFERENCES**

- 1. Lunyera J, Mohottige D, Isenburg MV, Jeuland M, Patel UD, Stanifer JW. CKD of Uncertain Etiology: A Systematic Review. *Clin J Am Soc Nephrol.* 2016;11:379-85.
- 2. Wesseling C, Crowe J, Hogstedt C, Jakobsson K, Lucas R, Wegman D, editors. Mesoamerican Nephropathy: Report from the First International Research Workshop on MeN. San Jose, Costa Rica: Central American Institute for Studies on Toxic Substances (IRET-UNA), Program on Work, Environment and Health in Central American (SALTRA); 2013.
- 3. Correa-Rotter R, Wesseling C, Johnson RJ. CKD of unknown origin in Central America: the case for a Mesoamerican nephropathy. *Am J Kidney Dis.* 2014;63:506-20.
- Wijkstrom J, Leiva R, Elinder CG, Leiva S, Trujillo Z, Trujillo L, et al. Clinical and pathological characterization of mesoamerican nephropathy: a new kidney disease in central america. *Am J Kidney Dis*. 2013;62:908-18.
- Nanayakkara S, Komiya T, Ratnatunga N, Senevirathna ST, Harada KH, Hitomi T, et al. Tubulointerstitial damage as the major pathological lesion in endemic chronic kidney disease among farmers in North Central Province of Sri Lanka. *Environ Health Prev Med*. 2012;17:213-21.
- Lopez-Marin L, Chavez Y, Garcia XA, Flores WM, Garcia YM, Herrera R, et al. Histopathology of chronic kidney disease of unknown etiology in Salvadoran agricultural communities. MEDICC Rev. 2014; 16:49-54.
- Torres C, Aragon A, Gonzalez M, Lopez I, Jakobsson K, Elinder CG, et al. Decreased kidney function of unknown cause in Nicaragua: a community-based survey. Am J Kidney Dis. 2010;55:485-96.
- Sanoff SL, Callejas L, Alonso CD, Hu Y, Colindres RE, Chin H, et al. Positive association of renal insufficiency with agriculture employment and unregulated alcohol

- consumption in Nicaragua. *Ren Fail*. 2010;32: 766-77.
- O'Donnell JK, Tobey M, Weiner DE, Stevens LA, Johnson S, Stringham P, et al. Prevalence of and risk factors for chronic kidney disease in rural Nicaragua. Nephrol Dial Transplant 2011;26:2798-805.
- Laux TS, Bert PJ, Barreto Ruiz GM, Gonzalez M, Unruh M, Aragon A, et al. Nicaragua revisited: evidence of lower prevalence of chronic kidney disease in a high-altitude, coffee-growing village. J Nephrol. 2012;25:533-40.
- Orantes CM, Herrera R, Almaguer M, Brizuela EG, Nunez L, Alvarado NP, et al. Epidemiology of chronic kidney disease in adults of Salvadoran agricultural communities. MEDICC Rev. 2014;16:23-30.
- Peraza S, Wesseling C, Aragon A, Leiva R, Garcia-Trabanino RA, Torres C, et al. Decreased kidney function among agricultural workers in El Salvador. Am J Kidney Dis. 2012;59:531-40.
- Laws RL, Brooks DR, Amador JJ, Weiner DE, Kaufman JS, Ramirez-Rubio O, et al. Changes in kidney function among Nicaraguan sugarcane workers. Int J Occup Environ Health. 2015;21:241-50.
- 14. Trabanino RG, Aguilar R, Silva CR, Mercado MO, Merino RL. End-stage renal disease among patients in a referral hospital in El Salvador. *Rev Panam Salud Publica*. 2002;12:202-6.
- 15. Krznaric R. The Limits on Pro-poor Agricultural Trade in Guatemala: Land, Labour and Political Power. *J Hum Dev.* 2006;7:111-35.
- Laux TS, Barnoya J, Guerrero DR, Rothstein M. Dialysis enrollment patterns in Guatemala: evidence of the chronic kidney disease of non-traditional causes epidemic in Mesoamerica. BMC Nephrol. 2015;16:54.
- 17. Keane WF, Brenner BM, de Zeeuw D, Grunfeld JP, McGill J, Mitch WE, et al. The

- risk of developing end-stage renal disease in patients with type 2 diabetes and nephropathy: the RENAAL study. *Kidney Int.* 2003;63:1499-507.
- 18. Phimda K, Hoontrakul S, Suttinont C, Chareonwat S, Losuwanaluk K, Chueasuwanchai S, et al. Doxycycline versus azithromycin for treatment of leptospirosis and scrub typhus. *Antimicrob Agents Chemother.* 2007;51:3259-63.
- 19. CPC.UNC.edu [Internet]. United States Agency for International Development (USAID): Quick Poverty Score Toolkit User's Guide - Guatemala [cited 2015 Oct]. Available from: http://www.cpc.unc. edu/measure/tools/poverty/ quick-poverty-score/QPS\_Guatemala\_ MS-09-35D.pdf
- Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009;150: 604-12.
- 21. Rahman M, Fu P, Sehgal AR, Smith MC. Interdialytic weight gain, compliance with dialysis regimen, and age are independent predictors of blood pressure in hemodialysis patients. *Am J Kidney Dis.* 2000;35: 257-65.
- 22. Weiner DE, McClean MD, Kaufman JS, Brooks DR. The Central American epidemic of CKD. Clin J Am Soc Nephrol. 2013;8:504-11.
- 23. Oj.Gob.Gt [Internet]. Guatemala National Institute of Statistics: Projection of Population by Municipality, 2008-2020 [cited 2015 Oct]. Available from: http://www.oj.gob.gt/estadisticaj/files/poblacion-total-por-municipio1.pdf
- 24. Delgado Cortez O. Heat stress assessment among workers in a Nicaraguan sugarcane farm. *Glob Health Action*. 2009;2: 10.3402/gha.v2i0.2069.
- 25. Orantes CM, Herrera R, Almaguer M, Brizuela EG, Hernandez CE, Bayarre H,

- et al. Chronic kidney disease and associated risk factors in the Bajo Lempa region of El Salvador: Nefrolempa study, 2009. *MEDICC Rev.* 2011;13:14-22.
- 26. Crowe J, Moya-Bonilla JM, Roman-Solano B, Robles-Ramirez A. Heat exposure in sugarcane workers in Costa Rica during the non-harvest season. *Glob Health Action*. 2010;3:10.3402/gha.v3i0. 5619.
- 27. Wesseling C, van Wendel de Joode B, Crowe J, Rittner R, Sanati, NA, Hogstedt C, et al. Mesoamerican nephropathy: geographical distribution and time trends of chronic kidney disease mortality between 1970 and 2012 in Costa Rica. Occup Environ Med. 2015;72:714-21.
- 28. Miranda JJ, Herrera VM, Chirinos JA, Gomez LF, Perel P, Pichardo R, et al. Major cardiovascular risk factors in Latin

- America: a comparison with the United States. The Latin American Consortium of Studies in Obesity (LASO). *PLoS One.* 2013;8:e54056.
- Johnson RJ, Glaser J, Sanchez-Lozada LG. Chronic kidney disease of unknown etiology: a disease related to global warming? MEDICC Rev. 2014;16:79-80.
- 30. PAHO.org [Internet]. Washington D.C.: Chronic kidney diseases (N18) and Renal failure (N17-N19) mortality, countries of the Americas (Age-standardized mortality rate per 100,000 population) [cited 2015 Oct]. Available from: http://www.paho.org/hq/index.php?option=com\_content&view=article&id=9402
- 31. Tonelli M, Pannu N, Manns B. Oral phosphate binders in patients with kidney failure. *N Engl J Med.* 2010;362: 1312-24.

- 32. Kalantar-Zadeh K, Gutekunst L, Mehrotra R, Kovesdy CP, Bross R, Shinaberger CS, et al. Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. *Clin J Am Soc Nephrol.* 2010;5:519-30.
- 33. PAHO.org [Internet]. Washington D.C.: Health Systems Profile Guatemala [cited 2015 Oct]. Available from: http://www2. paho.org/hq/dmdocuments/2010/Health\_ System\_Profile-Guatemala\_2007.pdf

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# **RESUMEN**

Prevalencia de enfermedad renal crónica por causas no tradicionales en pacientes en hemodiálisis en el sudoeste de Guatemala *Objetivo*. Documentar la prevalencia de enfermedad renal crónica por causas no tradicionales en los pacientes en hemodiálisis en el sudoeste de Guatemala.

Métodos. En este estudio descriptivo y transversal se entrevistó a pacientes en hemodiálisis en el Instituto Guatemalteco de Seguridad Social para obtener datos sobre su salud y antecedentes ocupacionales. Los datos de las pruebas de laboratorio séricas y de orina y los signos vitales al inicio de la hemodiálisis se extrajeron de los expedientes clínicos. Para clasificar a los pacientes se tomó en cuenta si eran hipertensos u obesos, o ninguna de las dos cosas. Se registró la proporción de pacientes con estos factores de riesgo tradicionales de enfermedad renal crónica y sin ellos, y se analizó la asociación entre los factores demográficos y ocupacionales y la falta de factores de riesgo tradicionales utilizando métodos de regresión logística multifactorial. Resultados. De un total de 242 pacientes que recibían hemodiálisis en el sudoeste de Guatemala (incluidos 171 que no eran diabéticos), 45 carecían de factores de riesgo tradicionales de enfermedad renal crónica (18,6% del total de pacientes y 26,3% de pacientes sin diabetes). A pesar de que los antecedentes de trabajo agrícola eran comunes, solo el tiempo de viaje superior a 30 minutos y la edad inferior a los 50 años se asociaron significativamente con enfermedad renal crónica cuando estaban ausentes los factores de riesgo tradicionales. Las personas en las que no se detectaron estos factores de riesgo tradicionales vivían en cinco departamentos del sudoeste de Guatemala.

Conclusiones. La prevalencia de enfermedad renal crónica por causas no tradicionales aparentemente es muy inferior en esta muestra de pacientes que reciben hemodiálisis en el sudoeste de Guatemala que en los pacientes hospitalizados en El Salvador. Todavía no se ha determinado si la prevalencia es mayor en la población general y en los pacientes que reciben diálisis peritoneal.

Palabras clave

América Central; insuficiencia renal crónica; diálisis; Guatemala.